Biotech Daily

Friday July 14, 2023

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market was up 0.78 percent on Friday July 14, 2023, with the ASX200 up 56.2 points to 7,303.1 points. Twenty-three of the Biotech Daily Top 40 stocks were up, nine fell, five traded unchanged and three were untraded.

Medical Developments was the best for the second day in a row, on no news, up 27 cents or 22.2 percent to $1.485, with 466,349 shares traded, followed by Patrys up 20 percent to 1.2 cents with 3.8 million shares traded.

Neuren climbed 16.75 percent; Avita was up 15.6 percent; Universal Biosensors improved 13.6 percent; Volpara was up 11.9 percent; Orthocell rose 9.9 percent; Mesoblast was up 8.2 percent; Pharmaxis climbed 7.8 percent; Alcidion, Prescient and Telix were up more than five percent; Polynovo, Resonance and Starpharma were up more than four percent; Immutep and Paradigm improved more than three percent; Actinogen, Next Science and Opthea rose more than two percent; Cochlear climbed one percent; with Clinuvel and Pro Medicus up by less than one percent.

Kazia led the falls, down 0.2 cents or 5.3 percent to 3.6 cents, with 2.9 million shares traded. Atomo and Impedimed lost more than five percent; Emvision fell 4.8 percent; 4D Medical shed 3.6 percent; CSL, Resmed and SDI were down more than one percent; with Cyclopharm, Nanosonics and Proteomics down by less than one percent.

DR BOREHAM'S CRUCIBLE: AROVELLA THERAPEUTICS

By TIM BOREHAM

ASX code: ALA

Share price: 4.7 cents; **Shares on issue:** 899,149,698; **Market cap:** $42.3 million

Chief executive officer: Dr Michael Baker

Board: Dr Tom Duthy (chair), Dr Baker, David Simmonds, Dr Debora Barton, Dr Elizabeth Stoner, Gary Phillips

Financials (March quarter 2023): receipts $19,000, net cash outflows $1.83 million, cash on hand - about $8 million post-raising.

Identifiable major shareholders: Merchant Funds Management 11.3%, Richard Mann (Mann Beef Pty Ltd) 6.4%

Little by little, investor purse strings are re-opening and biotechs are raising capital again. But their efforts are in dribs and drabs and no-one is aiming too high.

An exemplar is Arovella, the cancer immunotherapy play that raised $4.1 million and strived for an additional $1 million by way of a share purchase plan (SPP).

As it happened, on Tuesday the company announced the SPP had raised $2.2 million and - yes - the company would keep the over-subscription bestowed by the biotech gods.

Formerly the oral drug delivery developer Suda, Arovella has re-invented itself with a singular focus on the sexy immunotherapy discipline of Car-T therapies.

The Monty Python catchphrase - "and now for something completely different" - comes to mind.

Put another way, the company is like grandpa's axe with a new management, new board and a new raison d'etre within the old entity.

With a long-time interest in immunotherapies, Paul Hopper took over as chair of the then Suda in 2019. The country's busiest biotech entrepreneur declared the company was pursuing too many small programs without a commercial focus.

Still, little did we know that Suda/Arovella would pitch its spray mist delivery program completely, in favour of the Car-T program. But it did.

But one must angle where the fish are biting and investors have been lured by the pre-clinical results pertaining to Arovella's lead compound, called ALA-101, which targets a cancer marker called CD19 (see below).

Don’t quiver, it’s Arovella

The name Arovella derives from arrow (as in targeted drug delivery) and novel (as in new therapies).

Arovella plays in Car-T therapies alongside the ASX-listed Chimeric Therapeutics, Imugene and Prescient Therapeutics. (All of which just happen to be, or were, Paul Hopper-related companies.) ‘Car’ stands for chimeric antigen receptor and T refers to T-cells.

Arovella’s program revolves around invariant natural killer T-cells (iNKT) assets, acquired from Imperial College London. The company also has technology that targets a cancer marker called DKK1, acquired from the Houston, Texas-based MD Anderson Cancer Centre. The idea is eventually to use this in conjunction with the iNKT platform.

Arovella was initially known as Eastland Medical, which was incorporated in 1999 and listed in 2001, developing the sublingual Artimist as a treatment for malaria. The troubled Eastland changed its name to Suda in 2012, with a remit to develop spray-based oral delivery Oromist platform.

Mr Hopper’s appointment resulted in the departure of chief executive Stephen Carter after nine years at the helm, to be replaced by Dr Michael Baker, who was an investment manager with Bioscience Managers and is on the board of the Mr Hopper-chaired nuclear medicine play Radiopharm Theranostics.

In October 2021, Suda changed its name to Arovella. A year later, the company said it would cease development of Oromist and close its Perth facility.

Mr Hopper quit the board in June 2022, with Dr Thomas Duthy eventually taking his place as chair. Mr Hopper continues to chair Chimeric Therapeutics, which is also Car-T driven.

With about five staff, Arovella operates on a pure virtual model by which trials and pre-clinical work are outsourced.

Fighting the scourge of cancer - and acronyms

In June 2021, Arovella signed a deal with Imperial College London to acquire a cell therapy platform called invariant natural killer T-cells, or iNKT. The body’s strongest immune cells, iNKTs are a rare variant of T-cells.

Dr Baker said the program appealed because of Imperial College’s lofty status and the laboratory-ready nature of the asset.

Separately, the MD Anderson Cancer Centre delivered a poetically monikered asset called DKK1-Car/mAb. This peptide is the first to target DKK1, a biomarker of several forms of blood and solid cancers.

Dr Baker describes iNKT cells as “one of the most potent, naturally occurring immune cells.” (A mAb is a monoclonal antibody.)

Tackling blood cancers

Arovella's lead program, ALA-101, is showing early promise as a treatment for CD19-expressing blood cancers.

In April this year, the company's shares went on a mini-run after pre-clinical data was aired at the American Association of Cancer Research (AACR) in April.

In the mouse study, the rodents were infused with CD19-expressing, aggressive B-cell acute lymphoblastic leukemia cells. At the 90-day mark, only the 38 mice treated with ALA-101 (Car19-iNKT cells) and other Car-T therapies survived.

Of the 19 mice treated with ALA-101, the 90-day rate was 1.5 times better than the other Car-T mice and 90 percent of them were still squeaking.

An interesting twist is that four of the ALA-101 mice developed subsequent brain tumors, but they cleared up without further treatment. This suggests the effect of ALA-101 is enduring and that the molecule can cross the blood-brain barrier.

Crucially, the studies have shown the iNKT cells can be expanded by a factor of 5,000 without losing their potency.

"The data has given us great comfort that our proprietary manufacturing process allows for sufficient expansion of the iNKT cells that retain their functionality," Dr Baker says.

He adds that the first-generation Car-T therapies have resulted in significant relapses and safety risks such as cytokine release syndrome, neurotoxicity and infection.

"We believe there is a significant unmet need and ALA-101 is well placed to fill that need by having an off-the-shelf strategy to treat B cell lymphomas and leukemia."

. … and solid cancers

Arovella also has a joint program with the ASX-listed Imugene, which combines ALA-101 with Imugene's Oncarlytics therapy (more formally known as CF33-CD19).

This effort is relevant for solid cancers which - unlike blood cancers - do not exhibit the CD19 marker.
As Dr Baker says the Oncarlytic virus infects the cancer cells and forces them to express CD19. "Our iNKT cells will come along like heat-seeking missiles and find and destroy them," Dr Baker says.

The Imugene therapy also aims to kill the tumor cells. So, like Harpic Flushmatic dual action cistern blocks, there is a two-fold efficacy by combining both therapies.

This collaboration is in proof-of-study, in-vitro stage, with animal data expected in the second half of 2023.

Bespoke versus off-the-shelf

The usual Car-T manufacturing process involves blood being taken from a patient's arm. The T-cells are collected and are genetically reprogrammed to produce millions of chimeric antigen receptors.

The souped-up cells are infused back into the patient, where they define the cancer cells and trigger their destruction.

A point of (polite) debate in the Car-T community is whether the cells should be acquired from the patient (the autologous approach) or derived from healthy people and prepared as off -the-shelf therapy (allogeneic).

All six Car-T approved therapies to date are autologous.

Dr Baker says the pharmaceutical industry is not set-up for the bespoke (autologous) approach, resulting in high manufacturing costs and supply chain issues.

"As the starter cells come from a diseased patient, there are problems with immune compromise," he says.

"It also takes about four to six weeks to prepare the therapies and not all cancer centres are able to get access to them. Patients might succumb to the diseases while waiting for the treatment."

Arovella also has an option with the University of North Carolina, which involves licencing cytokine technology for the company's iNKT program.

The cell therapy sector's answer to Viagra, the program could result in potent and longer-lasting iNKT cells.

Finances and performance

Given the ratty market, Arovella has been a dab hand at raising capital under new management.

In January, the company raised $4.57 million in a placement at 3.8 cents a share, with biggest shareholder Merchant Funds chipping in $3 million. An underwritten, oversubscribed share purchase plan raised a further $1.5 million.

The latest placement secured $4.1 million at 4.5 cents, a 10 percent discount to the then prevailing price, followed by a share purchase plan that raised an additional $2.2 million.

As at the end of the March, the company had cash of $3.25 million, so the raising means it should be well endowed to meet its short-term goals.

Arovella shares were trading at a record low of two cents at the start of 2023, peaking at 10.5 cents in mid-April after the AACR prezzo.

Hits and misses

Arovella is the only Australian company working on an iNKT therapy - and only one of three or four globally.

In May, the Buffalo, New York based Athenex Inc entered voluntary bankruptcy protection after the US Food and Drug Administration placed its phase I program on clinical hold (after a patient died). Athenex bought its relevant asset for $US185 million two years previously and already owed $US250 million to Oaktree Capital (as with Arovella, the company had reinvented itself).

Others are the Nasdaq-listed, $US76 million market cap Mink Therapeutics (in phase I stage) and the private, pre-clinical Appia Biotech. In 2021, Appia signed a $US875 million deal with cell therapy leader Kite Pharma, so its shareholders could not have been ‘appier.

In the broader Car-T space, there are dozens of drug developers and no shortage of big-ticket deals.

In May this year, Janssen and Cellular Biomedicines Group announced a phase IIb collaboration involving a $US245 million upfront.

In January, Astrazeneca acquired Neogene Therapies for $US200 million of upfront payments and $US120 million of milestones. In phase I stage, the same-but-different Neogene dabbles in a variant called T-cell receptor therapies that recognise intracellular targets such as mutations.

Dr Boreham’s diagnosis:

Dr Baker says Car-T therapies have revolutionised blood cancer treatment, “to the point where are using ‘cure’ and ‘cancer’ in the one sentence”.

He adds that patient experience elsewhere shows that patients who took the treatment 10 years ago are still cancer-free.

In the short term, Arovella will focus on optimizing its cell manufacturing and scaling it up, in view of gaining regulatory approval for a phase I Hodgkinson’s lymphoma trial. This background work does not sound especially exciting, but the acquisitive action in the Car-T sector shows that things can happen at an early development stage.

For those who last the arduous journey, the value of the Car-T drug market is expected to exceed $US60 billion by 2030. The two earliest-approved drugs - Yescarta and Kyriah - last year turned over $US1.1 billion and $US500 million, respectively. Approved in 2021, Abecma achieved more than $US400 million in revenue.

“It’s a very promising sector that is set to get a lot bigger,” Dr Baker says.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He is in a very promising sector that is set to get a lot bigger – or so he has been told all his life.

NEUREN PHARMACEUTICALS

Neuren says Acadia will pay $US100 million ($145.1 million) upfront plus milestone payments of up-to $US427 million ($A619.5 million) to take its trofinetide licence global.
In 2019, Neuren said the San Diego-based Acadia Pharmaceuticals offer for the rights to trofinetide for Rett syndrome outside North America "would not be in the interests of… shareholders" (BD: Feb 1, 2019).
The previous year, the company said Acadia would pay up to $630 million for the North American rights to trofinetide for neurological indications including Rett syndrome and Fragile X, with the first option for other territories (BD: Aug 7, 2018).
Today, Neuren said it would receive royalties on net sales of trofinetide.
The company said it had granted Acadia an exclusive, worldwide licence to develop and commercialize NNZ-2591 for Rett syndrome and Fragile X syndrome, with milestone payments and royalties identical to those for trofinetide.
Neuren said it retained worldwide rights to NNZ-2591 in other markets and was conducting phase II trials of NNZ-2591 for Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndromes, with the first results expected in December 2023.
Neuren chief executive officer Jon Pilcher said "the unique knowledge and expertise that the Acadia team has built from the successful development and commercialization of Daybue [trofinetide] in the US, as well as the established supply chain, places them in the ideal position to achieve the optimum outcome globally for all stakeholders".
The company said future payments relating to North American sales of trofinetide were unchanged, at up-to $US350 million in milestone payments and royalties ranging between 10 to 15 percent of net sales and one third of the value realized by Acadia from the US Food and Drug Administration voucher it was awarded.
Neuren said it was entitled to a share of any upfront and development milestones should Acadia sublicence trofinetide for any region outside North America.
The company said that under the deal it had an obligation not to develop NNZ-2591 or any other product for North America in an indication for which Acadia develops trofinetide, except for Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndrome.
Neuren climbed $1.95 or 16.75 percent to $13.59 with 2.6 million shares traded.

IMAGION BIOSYSTEMS

Imagion says it has placed its one-for-eight, rights issue at 1.7 cents a share shortfall of $1.97 million, raising all of the hoped-for $2.4 million.
In April, Imagion said the rights issue raised $412,903 of a hoped-for $2.4 million, leaving a $1,970,000 shortfall to be placed by July 14, 2023 (BD: Apr 19, 2023).
Imagion fell 0.3 cents or 13.0 percent to two cents with 99.65 million shares traded.

WOKE PHARMACEUTICALS

Woke Pharmaceuticals says it has ethics approval for a 15-patient, phase II trial of its 25mg synthetic psilocybin WP002 for prolonged grief.
Woke said the trial, titled psilocybin assisted supportive psychotherapy in the treatment of prolonged grief (Parting), intended to show recruitment feasibility, intervention acceptability, safety and proof-of-concept efficacy.
The company said the Queensland Institute Medical Research Berghofer's Prof Vanessa Beesley would be the principal investigator, with the trial jointly funded by the Institute and Woke.
Woke is a private company.

CLINUVEL PHARMACEUTICALS

Clinuvel says that Germany's University of Münster filed patents in breach of its signed covenants and it has recognized Clinuvel's ownership of the intellectual property.
Clinuvel said it had secured a family of patents and patent applications related to the use of melanocortin-based molecules for treatment of neuro-inflammatory and neurodegenerative diseases following "protracted legal proceedings" against the University of Münster.
The company said the University had issued a formal apology for breaching legal agreements related to Clinuvel's proprietary technology and knowledge.
Clinuvel said it had worked with the University since 2007 on its melanocortin development program, with signed contracts protecting the company's intellectual property and know-how.
The company said that following the full transfer of patents, further disorders would be investigated, evaluating melanocortins as safe and effective treatments.
Clinuvel said the patents covered the use of melanocortin-based drugs as therapies for neurodegenerative disorders, including multiple sclerosis, Alzheimer's disease, and other related central nervous system disorders.
Clinuvel chief scientific officer Dr Dennis Wright said it was "a most unfortunate and unnecessary use of our resources that we had to resort to lengthy legal proceedings against the University of Münster to see the patents assigned to Clinuvel as the University has now issued a public apology".
"Perhaps this case serves to forewarn that an innovative pharmaceutical company will need to act in all matters to protect its rights," Dr Wright said.
Clinuvel was up one cent or 0.06 percent to $17.72.

NOXOPHARM

Noxopharm says it has less than one quarter of cash, but operationally has about four quarters of cash flow due to a "a major organizational restructure".
In April, Noxopharm said it would sack staff, prioritize resources to Chroma and Sofra technologies and discontinue two Veyonda trials due to protracted timelines, low patient acceptance of suppositories and predicted cost increases, as well as reduce spending (BD: Apr 6, 2023).
Today, the company said it had a cash burn of $3,450,000 for the three months to June 30 with cash and cash equivalents of $2,974,000 compared to $14,011,000 at June 30, 2022.
Noxopharm said the operating cash flow for the quarter was significantly higher than forecast for upcoming quarters due to one-off costs associated with discontinuing the clinical trials.
Noxopharm fell 0.2 cents or 5.3 percent to 3.6 cents.

LUMOS DIAGNOSTICS HOLDINGS

The New York-based Lind Global Fund II says it has ceased its substantial shareholding in Lumos, selling 6,000,000 shares for $442,152 or 7.37 cents a share.
In 2022, Lumos said it had an $8 million, two-year, convertible note facility from Lind Partners and SBC Global Investment Fund (BD: Nov 21, 2022).
Today, Lind Global said it sold the shares between July 10 and 12, 2023.
On July 5, 2023 Lind said held 22,500,000 shares, and Biotech Daily calculates that Lind retains 16,500,000 shares or 4.03 percent of the company.
Lumos was unchanged at 6.4 cents with 16.2 million shares traded.

ANTISENSE THERAPEUTICS

Antisense has requested a trading halt “pending an announcement in relation to a proposed capital raising”.
Trading will resume on July 18, 2023 or on an earlier announcement.
Antisense last traded at 6.5 cents.